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This report is in regard to Dr. Kesari, date of birth 6/10/1942, for a neurological evaluation.

Dr. Kesari presents with concerns for memory loss and cognitive impairment.

He reports progressive memory loss starting approximately 10 years ago. This was initially noted with forgetting patient names. His wife noted that he was forgetting appointments. He states that he forgot to pay a bill in recent months that led to cancellation of a credit card.

Dr. Kesari has intermittently forgotten to take medications and has occasionally taken medications at incorrect doses. He has repeated conversations and questions. Sequencing, scheduling. This has been more notable over the past 1-2 years.

He reports some degree of anxiety in regard to family issue and his wife's illness. He denies frank depression and rather reports ongoing ruminations.

Dr. Kesari immigrated to the United States in 1976 after medical training, he underwent internal medicine training in Chicago for one year and subsequently moved to Charleston. He owned an outpatient practice in Madison, West Virginia. In approximately 2016 he opened a clinic in Danville, WV. He reports that his practice in Danville was designed to improve access to Suboxone in a rural community that had poor access to this type of opiate addition treatment.

In June 2018 his wife arrived in California for end-stage liver cancer treatment, and he traveled frequently to support her treatment including a prolonged hospitalization. In mid-

2018 he began to perform teleconference follow up clinical visits.

Dr. Kesari reports a family history of schizophrenia in his brother. His father and mother suffered from memory loss at approximately age 70.

Dr. Kesari smoked cigarettes until approximately age 60. He reports drinking 2 alcohol containing beverages drinks until approximately 10 years ago. He continues to drink alcohol on a social basis.

He reports driving and has trouble. He reports "getting lost at times" but is able to navigate well with a family memory or GPS aiding him.

His review of symptoms incudes insomnia and an inability to sleep through the night. He was diagnosed with obstructive sleep apnea and underwent an oral surgery approximately 15 years ago that improved his snoring.

He denies headache, vision loss, falls, or dizziness,

He reports a history of motor vehicle accident that occurred approximately 10 years ago that did not result in significant head trauma or headaches.

He was diagnosed with type 2 diabetes approximately 10 years ago and has been treated with metformin and glyburide. He reports that his diabetes was under poor control at one point and has a recent hemoglobin A1c at 7.3%. He describes a change in diet as a way of improving his blood sugars and describes the ramifications

His past medical history includes hyperlipidemia and hypertension. In 2002 he suffered a heart attack, and in 2007 he had a four vessel bypass surgery.

He takes aspirin 81 mg, carvedilol, glyburide, metformin, Synthroid, lisinopril, rosuvastatin.

Neurological testing

Blood pressure is 121/82, heart rate 63

This patient is in no acute distress.

This patient has an unstable tandem gait.

Romberg test is negative.

Normal reflexes were elicited.

Normal cranial nerve exam noted including normal extaocular movements, facial symmetry.

No pronator drift was noted.

Normal upper and lower extremity strength is noted on confrontation testing.

Sensation was intact throughout the upper and lower extremities aside from decreased vibratory sensation in large toes, typical for age.

Montréal cognitive assessment was performed. Total score 20/30. 0/5 recall, 4/5 repetition.

Normal fluent speech, appropriate affect.

Diagnosis

1. Moderate cognitive impairment
2. Microvascular neurdegenerative brain disease
3. Type 2 diabetes
4. Hypertension

Plan

1. Formal neurocognitive testing
2. Polysomnogram for history of obstructive sleep apnea
3. Recommend electroencephalogram
4. Return to my office clinic in 3-4 weeks for reevaluation

Discussion

Dr. Kesari presents with approximately 10-year history of cognitive decline. His impairments with memory and attention have not dramatically worsened over the past 2-3 years rather has been more slowly progressive over the past several years.

Given his decline in certain instrumental activities of daily living and score on the Montréal cognitive assessment, he will qualify for a diagnosis of moderate cognitive impairment. The Montrèal cognitive assessment is a proven tool at differentiating normal aging patients from those with vascular neurodegeneration (Ghafar, Miptah, & O'Caoimh, 2019). Dr. Kesari's score of 20/30 indicates impairment with domains of concentration and memory. There is disagreement in regard to the precise score to differentiate dementia from cognitive impairment and normal aging, but the general consensus is that a score of 23 or lower is diagnostic for milder stages of dementia (Hsu et al., 2015).

For researchers the Clinical Dementia Rating (CDR) scale provides a numerical description

of patients' level of neurological dysfunction (Lo, 2017). The CDR measures impairments noted in the domains of memory, orientation, judgement, community affairs such as work, home life and hobbies, and self-care, and patients are given a scale of one to five dependent on their dependence on others for assistance. Using the CDR scale, patients with normal aging will typically have a CDR scale score of 0, and patients with CDR scores of 1 would typically receive a dementia diagnosis. The threshold of a CDR of 0.5 would indicate cognitive impairment. Dr. Kesari was given a CDR of 0.7, indicating more significant impairment.

In terms of classification of Dr. Kesari's underlying diagnosis resulting in moderate cognitive impairment, it is my opinion that he more likely has a vascular dementia than classic Alzheimer's disease.

His 2018 and 2020 MRIs show global cortical atrophy that is not particularly localized to the temporal lobe hippocamupus as would be expected in Alzheimer's disease (Logue et al., 2011). Moreover, the pattern of white matter hyperintensities would be consistent with vascular dementia. The finding of global hypometabolism seen on the PET/CT performed on 1/17/20 are consistent with this diagnosis. Vascular dementia is a neurodegeneration disease that affects the functioning of white matter tracts that connect brain regions and result in impairments in concentration, memory, executive functioning, and organization.

Based on my clinical interview and cognitive screening tests, I would describe his cognitive impairments to be affecting domains of executive functioning, memory, and visuospatial functioning that would be most consistent with vascular dementia (Desmond 2004, Graham et al. 2004, Kertesz & Clydesdale 1994, Lafosse et al. 1997, Lamar et al. 1997).

Dr. Kesari has a number of risk factors that would predispose him to vascular dementia including hypertension, diabetes, cardiovascular disease, smoking history, and obstructive sleep apnea. Like Alzheimer's disease, vascular dementia is a progressive condition and eventually results in dementia and increased reliance on caregivers for activities of daily living. One implication of a diagnosis of cognitive impairment is that the transition to dementia is expected to be 10-12% per year (Petersen, Smith, & Waring, 1999).

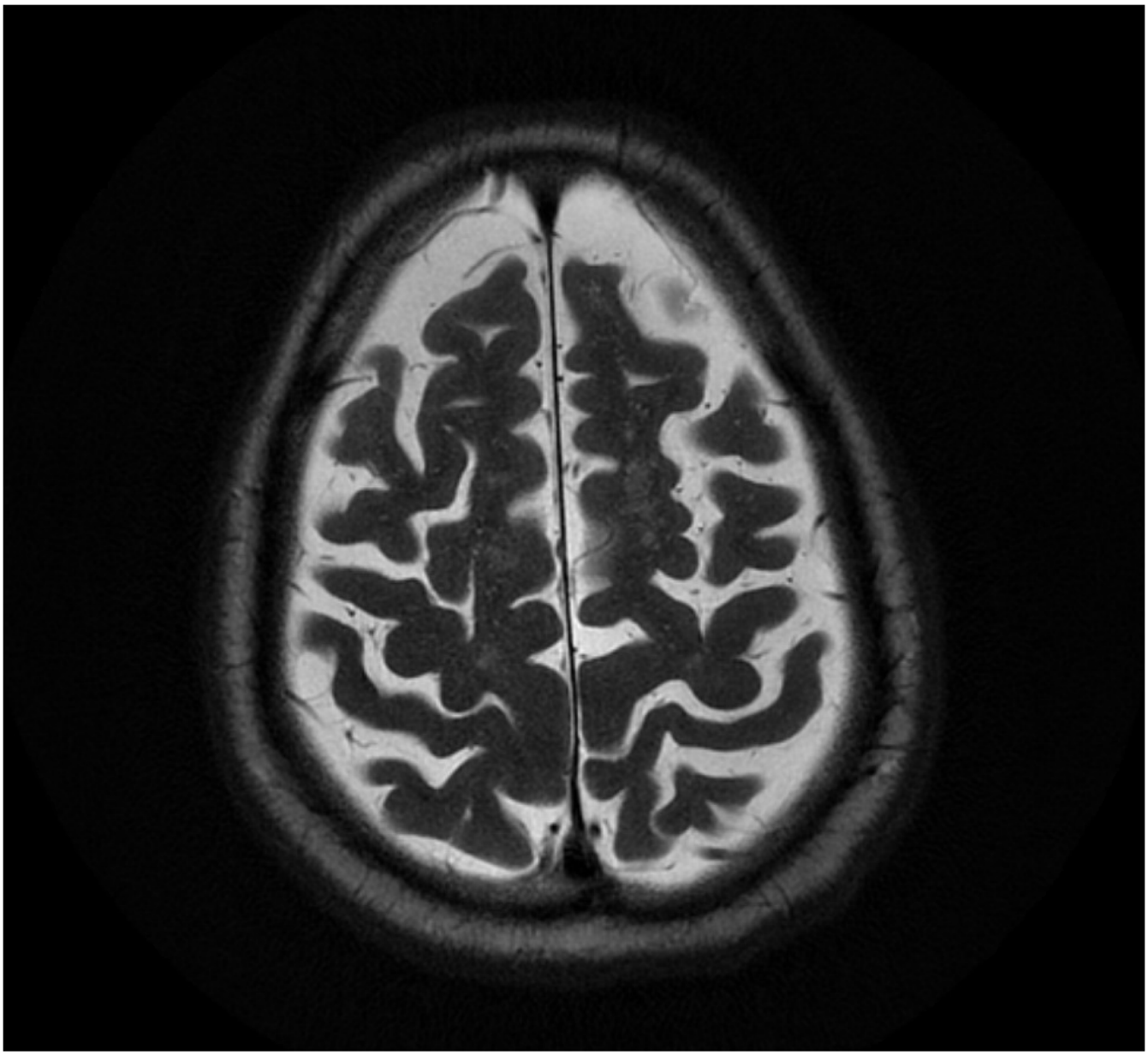
Based on review of the 2018 MRI brain, I can state with medical certainty that the same underlying disease process of vascular dementia was in place during this period in time, and I anticipate similar mild to moderate cognitive dysfunction as a result.

Thank you for allowing me to participate in this patient's neurologic care, please feel free to call us if there are any questions or problems.

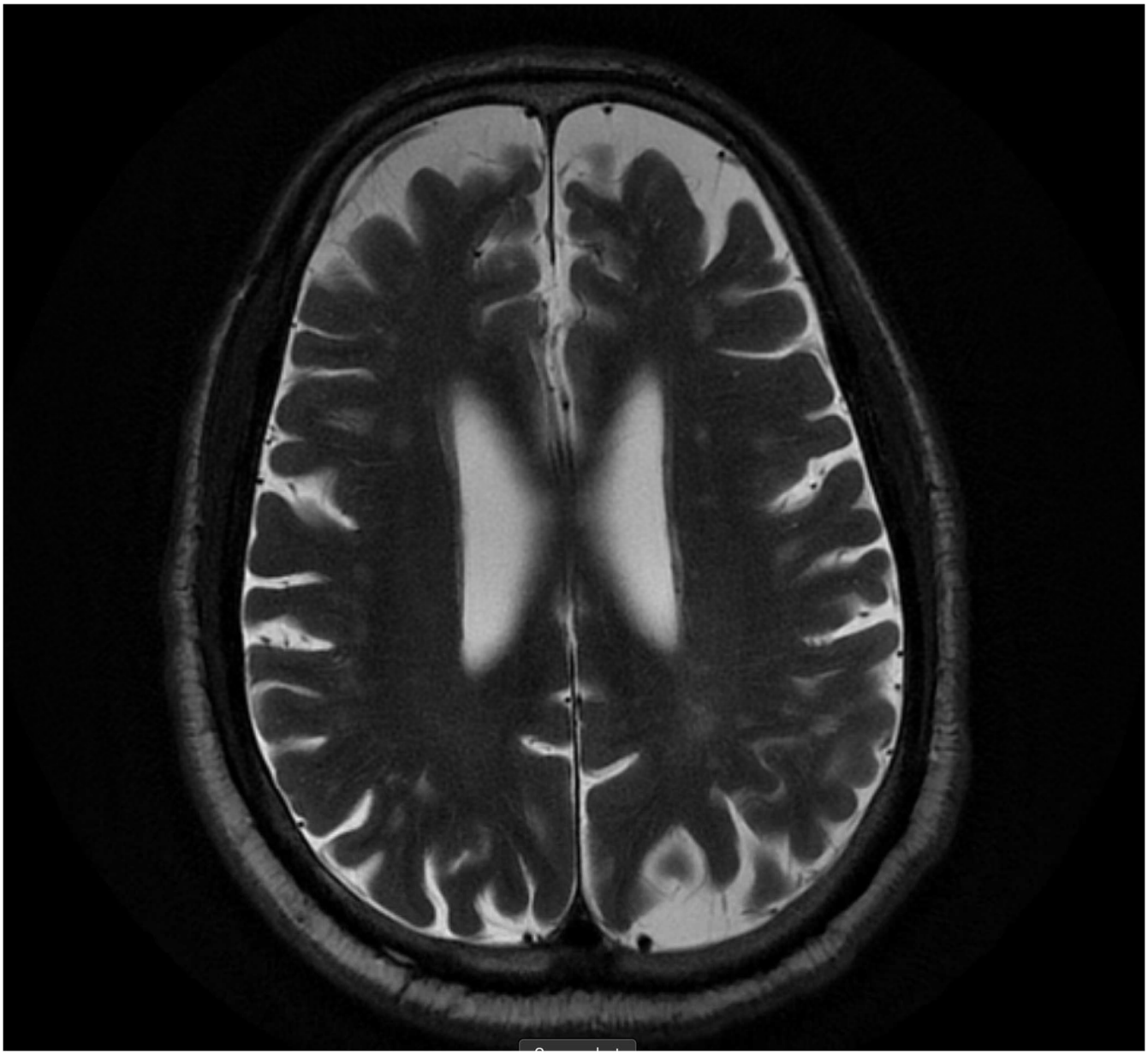
Sincerely,

Daniel T Franc, M.D., PhD.

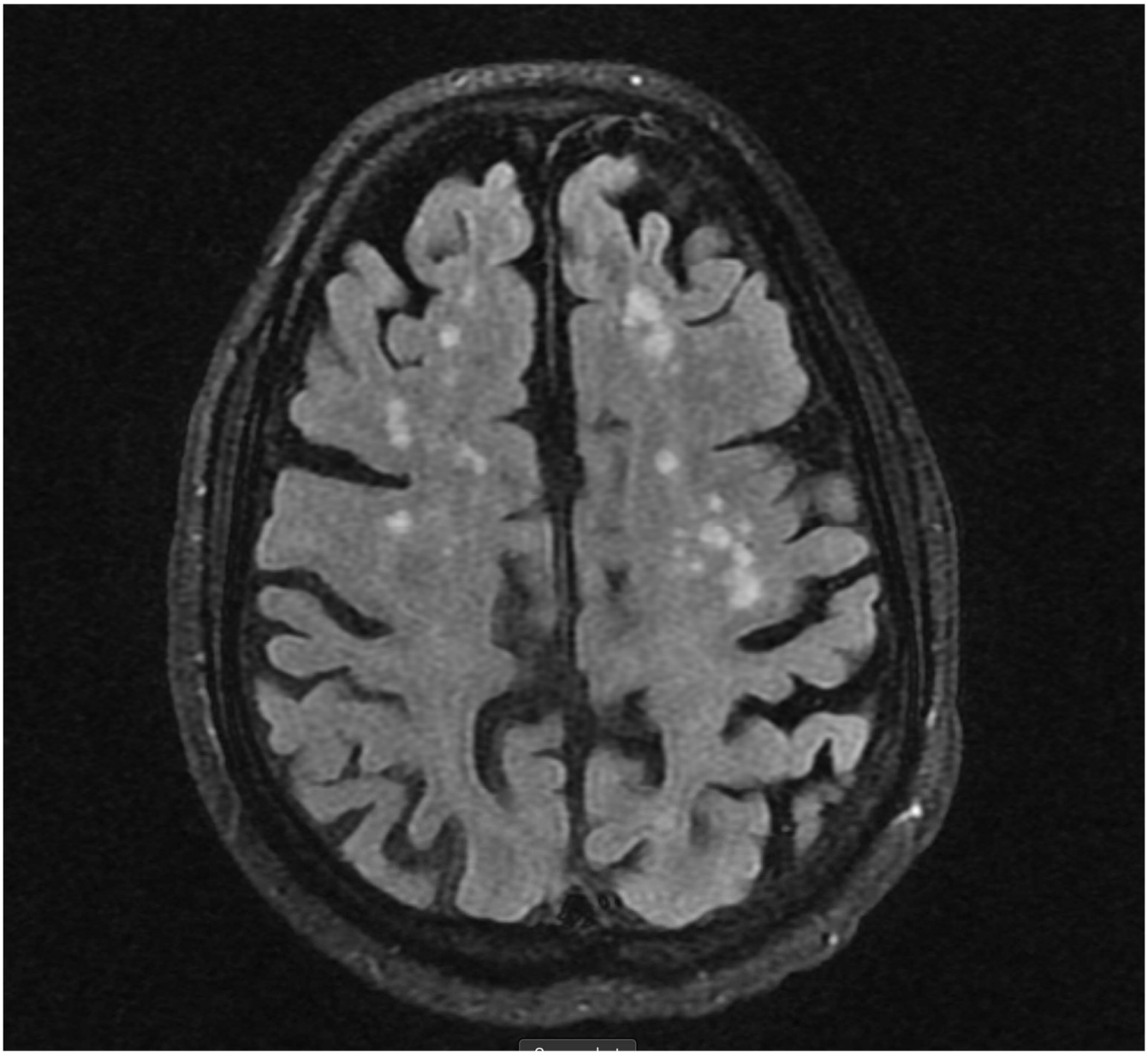
MRI brain 1/5/2020: Significant global cortical atrophy noted throughout the cerebrum.



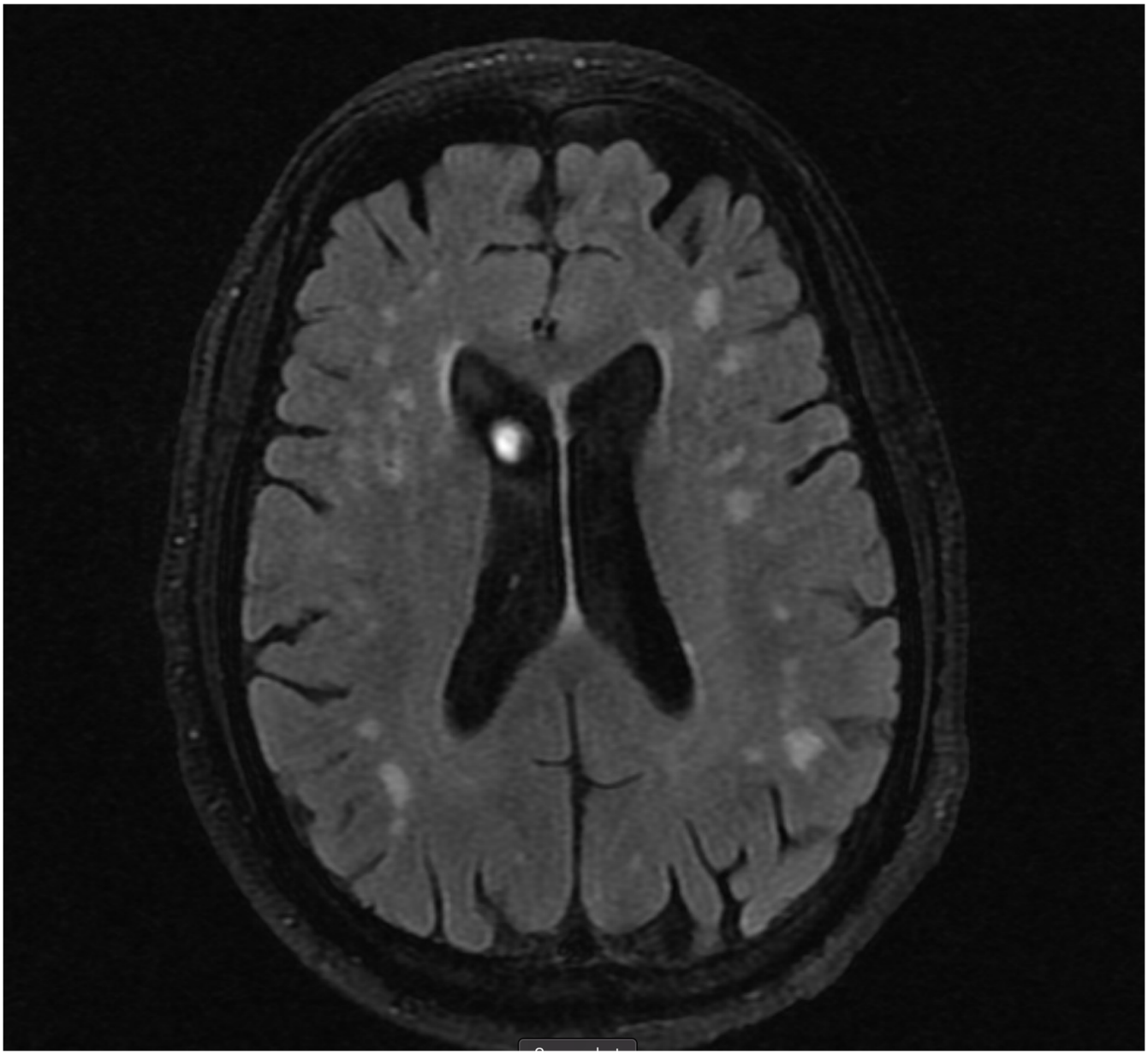
MRI brain 1/5/2020: Significant global cortical atrophy noted throughout the cerebrum, particular notable in the bilateral frontal lobes.



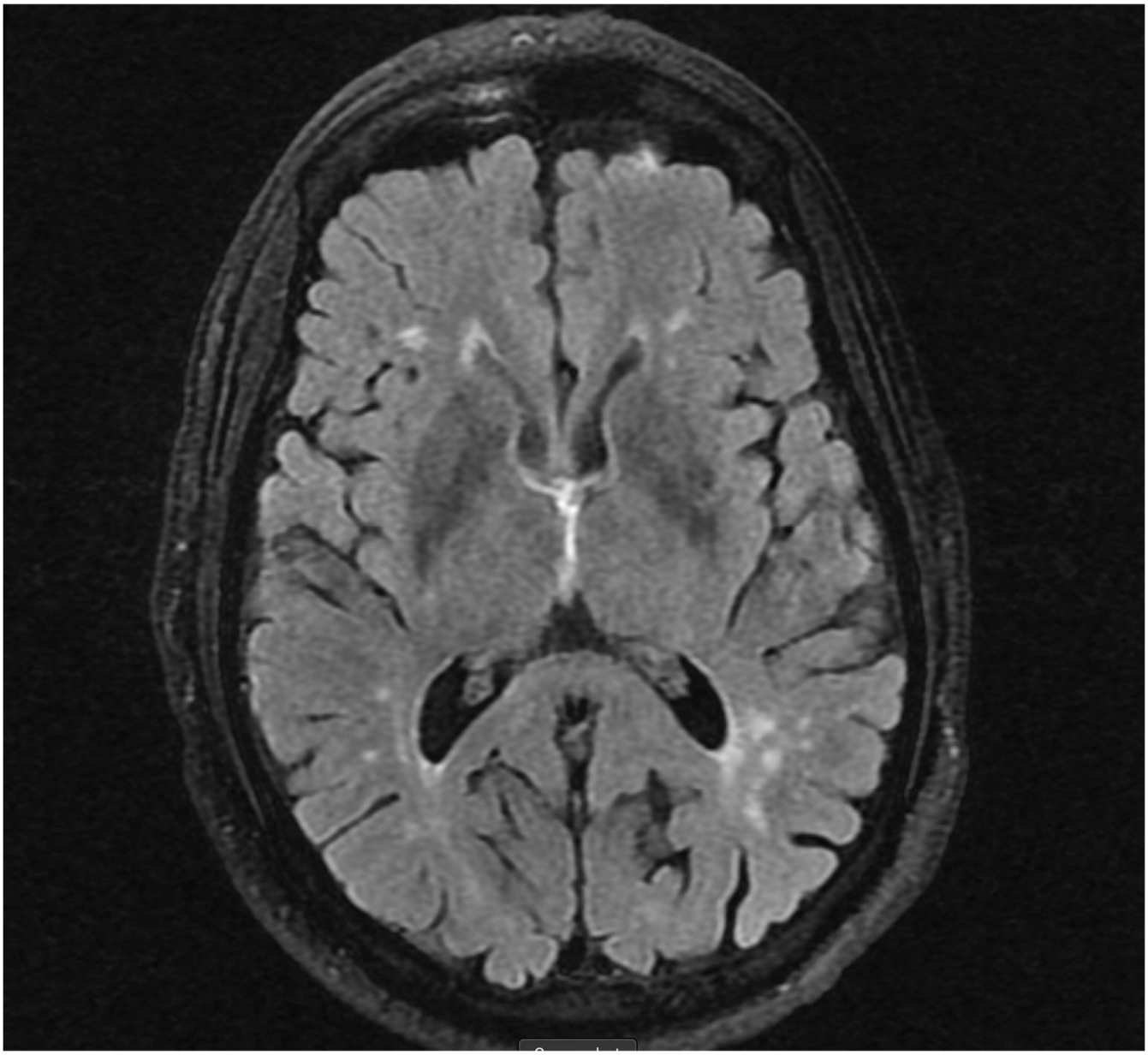
MRI brain 1/5/2020: White matter hyperintensities noted throughout deep white matter in both hemispheres.



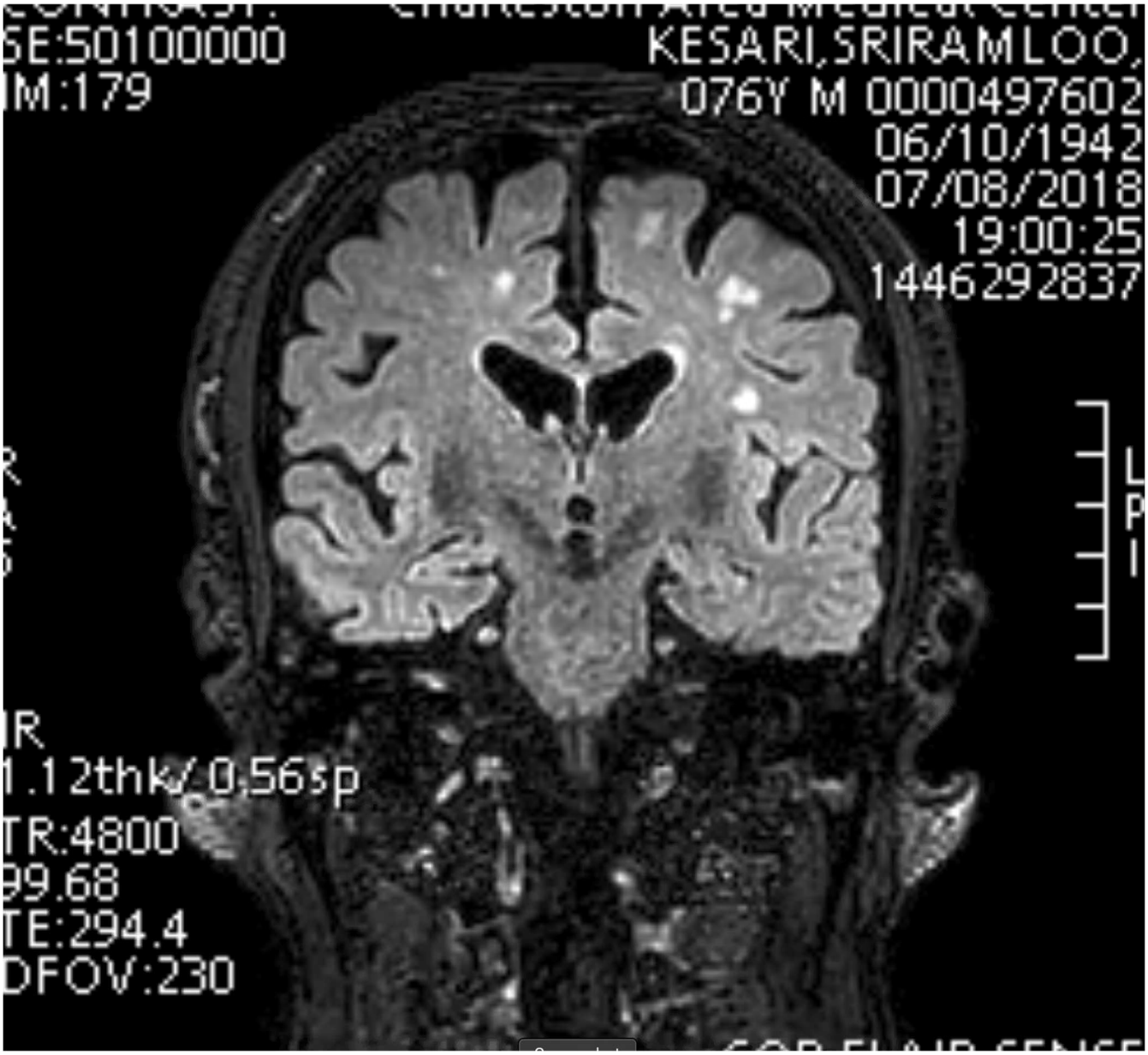
MRI brain 1/5/2020: White matter hyperintensities noted throughout deep white matter in both hemispheres.



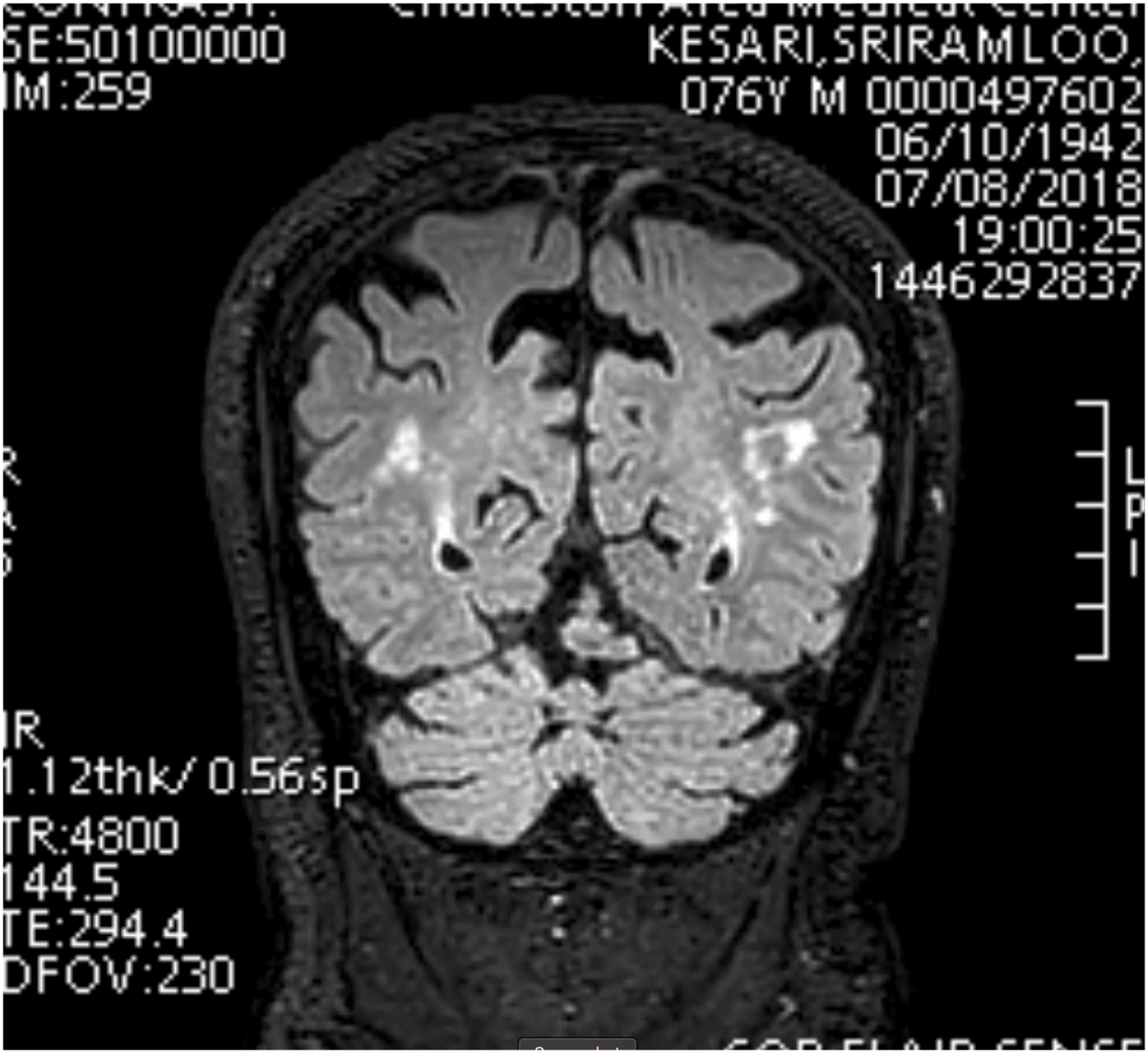
MRI brain 1/5/2020: White matter hyperintensities noted throughout deep white matter in both hemispheres.



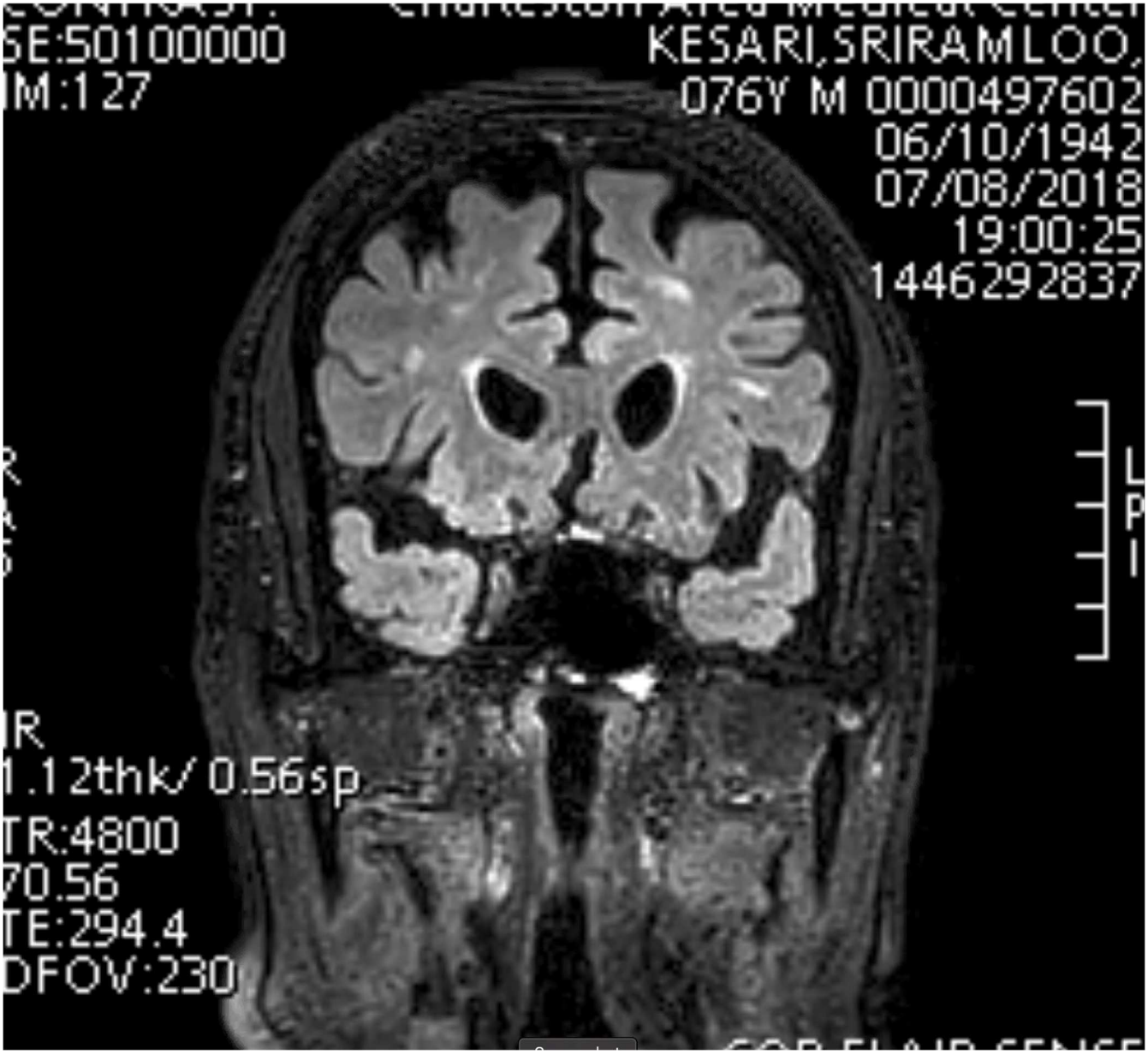
7/8/2018 MRI brain, without contrast: White matter hyperintensities noted in the deep white matter in both hemispheres.



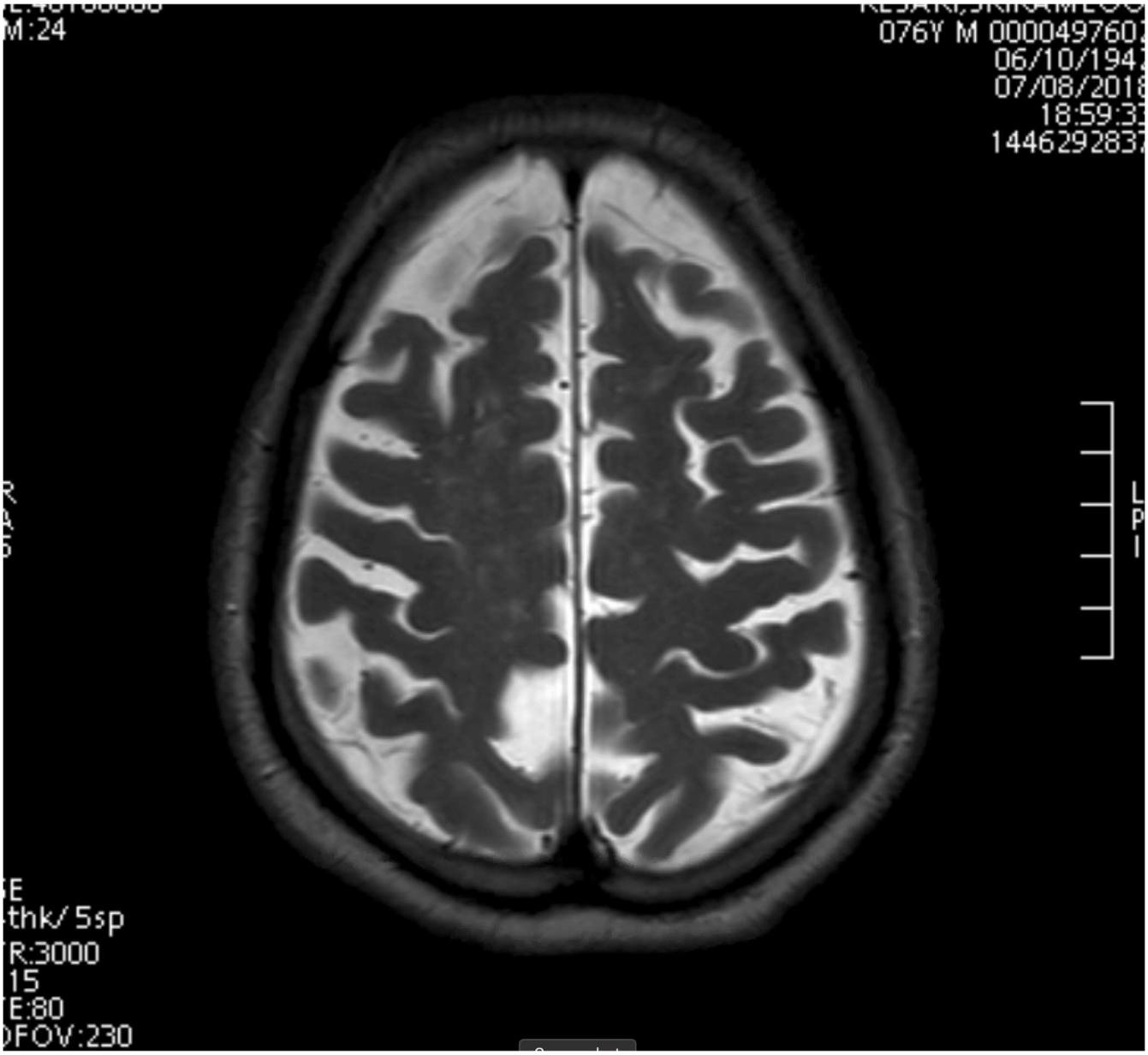
7/8/2018 MRI brain, without contrast: White matter hyperintensities noted in the deep white matter in both hemispheres. Cortical atrophy noted in bilateral cerebral hemispheres.



7/8/2018 MRI brain, without contrast: White matter hyperintensities noted in the deep white matter in both hemispheres. Cortical atrophy noted in bilateral cerebral hemispheres.



7/8/2018 MRI brain, without contrast: Cortical atrophy noted in bilateral cerebral hemispheres.



Bibliography

Ghafar, M. Z. A. A., Miptah, H. N., & O'Caoimh, R. (2019). Cognitive screening instruments to identify vascular cognitive impairment: A systematic review. *International Journal of Geriatric Psychiatry*, *34*(8), 1114–1127. https://doi.org/10.1002/gps.5136
Introduction: Vascular cognitive impairment (VCI) is common and important to detect as controlling risk factors, particularly hypertension, may slow onset and progression. There is no consensus as to which cognitive screening instrument (CSI) is most suitable for VCI. We systematically reviewed the psychometric properties of brief CSIs for vascular mild cognitive impairment (VMCI) and vascular dementia (VaD). Methods: Literature searches were performed using scholarly databases from inception until 31 May 2018. Studies were eligible if participants were aged 18 or older, interviewed face-to-face, and standard diagnostic criteria for VCI were applied, excluding those specifically identifying post-stroke dementia. Risk of bias was assessed using the Quality in Prognosis Studies (QUIPS) tool. Results: Fifteen studies were identified including eight types of CSIs (27 subtests/variants) and 4575 participants (1015 with VCI), mean age range: 51.6 to 75.5 years. Most studies compared more than one instrument. Five papers examined clock-drawing; four, the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE); and three used the Brief Memory and Executive Test (BMET). The MoCA (AUC > 0.90) and MMSE (AUC: 0.86-0.99) had excellent accuracy in differentiating VaD from controls; the MoCA had good internal consistency (Cronbach's α:.83-.88). The MoCA (AUC: 0.87-0.93) and BMET (AUC: 0.94) had the greatest accuracy in separating VMCI from controls. Most studies had low to moderate risk of bias in all domains of the QUIPS. Data were heterogeneous, precluding a meta-analysis. Conclusions: Although few studies were available and further research is required, data suggests that the MoCA is accurate and reliable for differentiating VaD and VMCI from controls.

Hsu, J. L., Fan, Y. C., Huang, Y. L., Wang, J., Chen, W. H., Chiu, H. C., & Bai, C. H. (2015). Improved predictive ability of the Montreal Cognitive Assessment for diagnosing dementia in a community-based study. *Alzheimer's Research and Therapy*, *7*(1). https://doi.org/10.1186/s13195-015-0156-8
Introduction: We compared the predictive ability of the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) to diagnose dementia in a community-based study. Methods: A total of 276 people aged 60 years or older were enrolled. All of the participants were administered face-to-face interview questionnaires and MoCA and MMSE examinations. The receiver operating characteristic curve method and area under curve were performed to assess the predictive ability for diagnosing dementia. Results: The 276 participants had a mean age of 67.9 ± 6.1 years and mean education duration of 11.4 ± 4.0 years. In general, the MoCA yielded higher AUCs (0.891) with favorable sensitivity (78 %) and excellent specificity (94 %) compared with the MMSE in differentiating the participants with and without dementia in either the total sample or all subgroups. Conclusion: Our study determined a higher predictive ability in the MoCA than in the MMSE for diagnosing dementia according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria in a community-based sample with a broader range of education level.

Lo, R. Y. (2017). The borderland between normal aging and dementia. *Ci Ji Yi Xue Za Zhi = Tzu-*

Chi Medical Journal. https://doi.org/10.4103/tcmj.tcmj_18_17
Alzheimer's disease (AD) has become a global health issue as the population ages. There is no effective treatment to protect against its occurrence or progression. Some argue that the lack of treatment response is due to delays in diagnosis. By the time a diagnosis of AD is made, neurodegenerative changes are at the stage where very few neurons can be salvaged by medication. The AD research community has developed the idea of mild cognitive impairment (MCI) in an attempt to find predementia patients who might benefit from potentially therapeutic drugs that have proven ineffective in the past. However, MCI is heterogeneous in terms of its underlying pathology and practicality for predicting dementia. This article first reviews the conceptual evolution of MCI as the borderland between normal aging and dementia, and then proposes that built environment and sociocultural context are two key elements in formulating a diagnosis of dementia. Dementia is more than a biomedical term. Cognitive impairment is considered a dynamic outcome of how an individual interacts with cognitive challenges. To focus on amyloid deposition as a single etiology for AD does not adequately capture the social implications and geriatric aspects of dementia. Moreover, MCI is nosologically questionable. Unlike a diagnosis of AD, for which a prototype has been well established, MCI is defined by operational criteria and there are no cases seen as typical MCI. Biofluid and imaging markers are under active development for early detection of amyloid deposition and neurofibrillary tangles in the brain, whereas vascular risks, chronic medical diseases, and polypharmacy continue to add to the complexity of dementia in old age. The paradigm of dementia care policy may shift to early diagnosis of AD pathology and comprehensive care for chronic diseases in the elderly population.

Logue, M. W., Posner, H., Green, R. C., Moline, M., Cupples, L. A., Lunetta, K. L., … DeCarli, C. (2011). MRI-measured atrophy and its relationship to cognitive functioning in vascular dementia and Alzheimer's disease patients. *Alzheimers Dement.*, *7*(5), 493–500. https://doi.org/10.1038/jid.2014.371
Recent pathological studies report vascular pathology in clinically diagnosed Alzheimer's disease (AD) and AD pathology in clinically diagnosed vascular dementia (VaD). We compared magnetic resonance imaging (MRI) measures of vascular brain injury (white matter hyperintensities (WMH) and infarcts) to neurodegenerative measures (medial-temporal atrophy (MTA) and cerebral atrophy (CA)) in clinically diagnosed subjects with either AD or VaD. We then examined relationships among these measures within and between the two groups and their relationships to mental status. Methods Semi-quantitative MRI measures were derived from blind ratings of MRI scans obtained from participants in a research clinical trial of VaD (N=694) and a genetic epidemiological study of AD (N=655). Results CA was similar in the two groups, but differences in the mean of MTA and WMH were pronounced. Infarcts were significantly associated with CA in VaD, but were not in AD; MTA and WMH were associated with CA in both. WMH was associated with MTA in both groups, however MRI infarcts were associated with MTA in VaD but not with MTA among AD patients. MTA was strongly associated with MMSE scores in both groups while evidence of a modest association between WMH and MMSE was seen among VaD patients. Conclusions MRI data from two dementia cohorts with differing dementia etiologies find that the clinical consequences of dementia are most strongly associated with cerebral and medial-temporal atrophy suggesting that tissue loss is the major substrate of the dementia syndrome. Keywords: Alzheimer's disease, MRI, Dementia, vascular, Hippocampus, Atrophy

Petersen, R. C., Smith, G. E., & Waring, S. (1999). Mild Cognitive Impairment. *Archives of Neurology*, *56*(6), 760. https://doi.org/10.1001/archneur.56.6.760
Background: Subjects with a mild cognitive impair- ment (MCI) have a memory impairment beyond that ex- pected for age and education yet are not demented. These subjects are becoming the focus ofmany prediction stud- ies and early intervention trials. Objective: To characterize clinically subjects with MCI cross-sectionally and longitudinally. Design: A prospective, longitudinal inception cohort. Setting: General community clinic. Participants: A sample of 76 consecutively evaluated subjects with MCI were compared with 234 healthy con- trol subjects and 106 patients with mild Alzheimer dis- ease (AD), all from a community setting as part of the Mayo Clinic Alzheimer's Disease Center/Alzheimer's Dis- ease Patient Registry, Rochester, Minn. Main Outcome Measures: The 3 groups of individu- als were compared on demographic factors and mea- sures ofcognitive function including the Mini-Mental State Examination, Wechsler Adult Intelligence Scale– Revised, Wechsler Memory Scale–Revised, Dementia Rat- ing Scale, Free and Cued Selective Reminding Test, and Auditory Verbal Learning Test. Clinical classifications of dementia and AD were determined according to the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition and the National Institute of Neu- rological and Communicative Disorders and Stroke– Alzheimer's Disease and Related Disorders Association criteria, respectively. Results: The primary distinction between control sub- jects and subjects with MCI was in the area of memory, while other cognitive functions were comparable. How- ever, when the subjects with MCI were compared with the patients with very mild AD, memory performance was similar, but patients withADwere more impaired in other cognitive domains as well. Longitudinal performance dem- onstrated that the subjects with MCI declined at a rate greater than that of the controls but less rapidly than the patients with mild AD. Conclusions: Patients who meet the criteria for MCI can be differentiated from healthy control subjects and those with very mild AD. They appear to constitute a clinical entity that can be characterized for treatment interven- tions. Arch